

# The NICHD Connection

*April 2019*

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## NICHD Exchange Recap: "Genome Editing: Rewriting Fate"

*By Shana R. Spindler, PhD*

In ancient Greek mythology, the three Fates determine the destiny of all mortals. These Goddesses stood in the backdrop, with DNA in hand, as staff and scientists gathered on January 31, 2019, to discuss how genome editing is allowing mortals to change destiny too. The four NICHD Exchange speakers explored the benefits and risks of a DNA editing technology known as CRISPR/Cas9. They focused on multiple topics, including the historical timeline of gene editing, examples of CRISPR in use at the NICHD, and the legal and moral implications of editing someone's genome.



CRISPR/Cas9 is a genome editing method that has been co-opted from the immune system of bacteria, requiring two major components: CRISPR and Cas9. Shorthand for Clustered Regularly Interspaced Short Palindromic Repeats, CRISPR DNA encodes small chunks of RNA, whereas Cas9 is a protein that cuts DNA. The encoded RNA is used to target Cas9 to viral genes for destruction in bacteria. But in the lab, scientists design custom CRISPR RNAs to target genes of interest.

When injected into living cells, the customized CRISPR/Cas9 complex seeks an exact match in the genome where it makes a double stranded cut, taking a target gene out of commission. Scientists have created modified versions of this system to instead fix and repair genes as well. The applications for this technology are far reaching.

A historical look at how we arrived at current genome editing techniques can

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## Letter from the Editor

If you haven't had the opportunity to attend an NICHD Exchange meeting, I highly recommend that you check one out. The topics are noteworthy, often coinciding with issues of general public interest. We [recap the first Exchange meeting](#) of the year for our feature article this month. The theme: genome editing. You've likely encountered genetic modification in the lab, on the news, or even in the grocery store. This Exchange meeting gave participants a platform to explore the risks and benefits of playing with DNA—especially our own.

While discussing one type of gene editing method, CRISPR/Cas9, my friend and I joked that CRISPR will one day become as rudimentary as PCR. No doubt, early career trainees stand at an exciting time in genetic research. So please join *The NICHD Connection* as we congratulate our [recent PhD graduates](#). We wish them well on their scientific journeys, equipped with technology that will open fascinating lines of investigation.

For those still in training, Suna Gulay's "[Rep Report](#)" and the [April announcements](#) deliver ways to engage in communication and career development opportunities on campus. Don't know where to start? Feel free to contact Drs. Yvette Pittman ([yvette.pittman@nih.gov](mailto:yvette.pittman@nih.gov)) or Erin Walsh ([erin.walsh@nih.gov](mailto:erin.walsh@nih.gov)) in the NICHD Office of Education. They are happy to help you identify opportunities that work for you!

Your Editor in Chief,  
Shana R. Spindler, PhD

Please send questions or comments to our editor at [Shana.Spindler@gmail.com](mailto:Shana.Spindler@gmail.com).



## NICHD Exchange Recap: “Genome Editing: Rewriting Fate”

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offer insight into where these cutting edge methods might lead in the future.

**Dr. Tim Petros**, principal investigator in the NICHD Unit on Cellular and Molecular Neurodevelopment, kicked off the meeting with his talk “Splicing & Dicing: The Future of Gene Editing.” He presented a brief history of genome modification and the decades of research at its foundation.

Today, most students know what DNA looks like by the end of a basic biology class. But before the early 1950s, no one did. Even with the helical structure in hand, scientists took more than a decade to discover how to cut and paste DNA with restriction enzymes and ligases. We didn’t gain the skills needed to copy and sequence DNA until, as Dr. Petros termed it, “the birth of molecular cloning.” This was a necessary step to understanding homologous recombination, our first peek at DNA editing. Eventually, scientists began to pursue more efficient ways to modify DNA: meganucleases, zinc finger nucleases, and TALEN entered the scene.

Humanity entered an era of reprogramming the living world around us. Dr. Petros presented a taste of our newfound ability, including food supply modification, livestock improvements, pathogen reduction, biofuel production, and human disease and treatment research.

Over the past two decades, the introduction of CRISPR/Cas9 has had an undeniable impact on the pace of research. The number of CRISPR/Cas9-containing studies published between 2005 and 2018 has grown at an astonishing rate, from just a few to several thousand. In 2013, the scientific community witnessed the first use of the CRISPR system in mammalian cells.<sup>1</sup> Just a year later, monkeys entered the world harboring CRISPR/Cas9 targeted mutations.<sup>2</sup> And today, multiple biotech companies are heavily invested in CRISPR technology, with ongoing Phase 1 clinical trials using CRISPR/Cas9 to treat human diseases.

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## NICHD Exchange Recap: “Genome Editing: Rewriting Fate”

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The historical achievements in genome editing have led to CRISPR/Cas9 playing a major role in basic science research worldwide. The second presenter of the meeting, **Dr. Mary Dasso**, senior investigator in the NICHD Section on Cell Cycle Regulation, shared the benefits of CRISPR/Cas9 in her work. During her talk “Trial in Absentia: Using Gene Editing to Understand Nucleoporin Function Through Regulated Degradation,” the audience learned about CRISPR/Cas9’s impact on her lab’s research scope and pace of progress.

Dr. Dasso uses CRISPR/Cas9 to study communication between the cytoplasm and nucleus. Her group focuses on the nuclear pore complex, “a hub of biological regulation” that is composed of multiple proteins called nucleoporins. Unfortunately, removing nucleoporins to study their function can affect cellular activities essential for survival, making research difficult. Adding to the complexity, Dr. Dasso aims to study most, if not all, nucleoporins. Creating a knock-out model for each protein is beyond the scope of a single lab—without CRISPR/Cas9 that is.

Dr. Dasso’s lab uses an elegant CRISPR-based system to study each protein within the complex without disrupting all cellular function. The team can modify any protein to include a tag that allows for inducible and targeted destruction of individual nucleoporins within two months. What makes this work exceptional is that the lab uses CRISPR/Cas9 to make genetic modifications at a scale and pace previously unseen. The progress was evident, revealing some surprising roles of nuclear pore members in chromosome organization and transcription.

The CRISPR system permits greater research scope and speed, but also brings in unique legislative restrictions when used in humans. **Dr. Stuart Moss**, a health scientist administrator in the NICHD Fertility and Infertility Branch, highlighted the legislative concerns of using CRISPR/Cas9 in human research in his talk about male infertility, “Men Are Not so Simple: So Many Spermatogenic Genes, so Little Time (To Knock Them Out).”

Male infertility is complex. Between one to two thousand genes are involved in spermatogenesis (that’s somewhere between five to ten percent of the human genome!). With so many genes involved, fertility can be affected due to disruptions

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## NICHD Exchange Recap: “Genome Editing: Rewriting Fate”

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to diverse aspects of development. Ongoing CRISPR/Cas9-based studies in mice are addressing one gene at a time. But while research in mice goes ahead, treating male infertility in humans brings with it additional complexity.

At this point in his talk, Dr. Moss switched gears from model system genetics to the legislative restrictions of gene editing technology in humans. There are two types of gene therapy: somatic cell and germline gene therapy. Human somatic cell gene therapy is allowed by the National Institutes of Health (NIH), and a common fund program has dedicated 190 million dollars over six years to its study. However, gene editing of human germline cells is different. Dr. Moss cited a legislative amendment rider (the Dickey-Wicker amendment) that prohibits the use of federal funds to create, destroy, discard or injure human embryos for research purposes. This regulation effectively prevents any research on human germline gene editing from receiving federal funding in the United States.

Dr. Moss also addressed the concern of privately funded human germline research. He explained that another amendment rider prohibits the FDA from reviewing or approving applications that include the creation or modification of human embryos with a heritable genetic modification. The combination of this and federal funding restrictions effectively prohibits germline gene therapies from being administered by any entity in the United States.

Given the germline’s involvement in fertility, and current legislative restrictions, researchers need to carefully design how they study and treat male infertility. Dr. Moss asked the question directly—can you fix male fertility without changing the germline? “The easy answer is no,” he said. But gene editing still has a place in male fertility research; not all infertility stems from germline problems. For example, researchers can use gene editing to address somatic cell defects, a non-germline contributor to infertility.

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## NICHD Exchange Recap: “Genome Editing: Rewriting Fate”

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Dr. Moss’ discussion on infertility research highlighted the complexity of gene editing technology use in humans. **Dr. Melissa Parisi**, chief of NICHD’s Intellectual and Developmental Disabilities Branch, wrapped up the meeting by continuing the discussion on genome editing’s benefits and risks. Her talk, “Gene Editing to ‘Fix’ Heritable Disorders in Children: Opening Pandora’s Box,” included applications of genome editing for specific genetic diseases, and concerns about this rapidly evolving technology.

Dr. Parisi presented multiple gene-editing success stories, but one stood out: a 2018 study using CRISPR/Cas9 to correct a Duchenne Muscular Dystrophy mutation in one-month-old Beagle puppies.<sup>3</sup> Upon CRISPR/Cas9-mediated therapy, the researchers observed tissue-dependent changes in dystrophin levels after only eight weeks. This included restoring dystrophin up to a striking 92% of normal levels in cardiac muscles. Studies like this in large animals suggest the potential clinical utility of gene editing in humans.

Although the benefits of genome editing are no doubt impressive, there are risks. Dr. Parisi offered a sobering reminder that gene therapy treatments aren’t always ideal. For one, genetic modifications might not be precise, creating off-target effects that could lead to unintended biological issues. In addition to unexpected effects, we must consider that a newfound ability to alter genes might create an “ethical slippery slope.”

We are nowhere near understanding the long-term consequences, both biological and societal, of using CRISPR to affect change in the human genome. This makes it all the more serious that a scientist in China has allegedly created genome-edited human babies using CRISPR, an act that [triggered a response](#) from the NIH Director, Dr. Francis Collins.

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## NICHD Exchange Recap: “Genome Editing: Rewriting Fate”

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The scientific community must find a way to balance the benefits and risks of human genome editing as we move forward with new technologies. To address these real concerns and at the same time bolster progress in genome editing, the NIH created the Common Fund Somatic Cell Genome Editing (SCGE) Program. By facilitating interactions between invested parties, the SCGE Program aims to improve necessary components in genome editing research, such as genome editing reagents, better animal models, and enhanced *in vivo* delivery tools. In addition, the program proposes an assessment of unintended biological effects and the coordination of partnerships to disseminate information.

Dr. Parisi ended her talk on a note of hope, not despair. With ample support for the scientific community and proper regulations in place to guide the way, we can mitigate the risks of genome editing and reap the rewards.

At the conclusion of the event, NICHD Director Dr. Diana Bianchi celebrated that genetics has gone from a diagnostic focus to one of treatment. She shared an impactful experience of hearing a grandmother talk about losing her first grandchild to muscular dystrophy, but then seeing her second grandchild treated and walking. “It’s such a timely topic...incredibly timely topic,” Dr. Bianchi emphasized to the crowd. We are neither gods nor goddesses, but with the emergence of genome editing tools like CRISPR/Cas9, we cannot deny that our fate is in our own hands.

### REFERENCES

1. Cong L, et al. Multiplex genome engineering using CRISPR/Cas systems. *Science*. 2013 Feb 15;339(6121):819-23.
2. Niu Y, et al. Generation of gene-modified cynomolgus monkey via Cas9/RNA-mediated gene targeting in one-cell embryos. *Cell*. 2014 Feb 13;156(4):836-43.
3. Amoasii L, et al. Gene editing restores dystrophin expression in a canine model of Duchenne muscular dystrophy. *Science*. 2018 Oct 5;362(6410):86-91.



## Congrats to our 2018 NICHD Graduates

Congratulations to the following NICHD graduates who completed the NIH Graduate Partnerships Program (GPP) last year:



**Dr. Emma Elizabeth Condry** graduated from Virginia Tech under the supervision of Dr. Bruce Friedman, with NICHD advisor Dr. Amir Gandjbakhche.

Doctoral thesis work: "Examining the Neurovisceral Integration Model through fNIRS."



**Dr. Rogers Alberto Nahui Palomino** graduated from the University of Bologna under the supervision of Dr. Beatrice Vitali, with NICHD advisor Dr. Leonid Margolis. He is continuing his work at the NICHD as a postdoctoral fellow in the Margolis lab and currently studies the protective mechanisms of Vaginal *Lactobacillus*, isolated from healthy women, against HIV-1 infection in human cervico-vaginal and lymphoid tissues *ex vivo*.

Doctoral thesis work: "Therapeutic Potential of Vaginal Lactobacilli for Women's Health: Interaction with Pathogens and Epithelium Cells."



# The Rep Report

By Suna Gulay, PhD

As the current NICHD Basic Sciences Institutes and Centers (IC) Representative, I represent NICHD postdoctoral fellows at the Fellows Committee ([FelCom](#)) meeting every month and share the latest news with you here. Do you have a concern or question that you want brought up at the next meeting? Contact me at [suna.gulay@nih.gov](mailto:suna.gulay@nih.gov)!



Dear fellows,

At the March meeting, Dr. Charles Dearolf of the Office of Intramural Research notified the FelCom of a 3% raise in trainee stipends, approved by Dr. Francis Collins starting May 1! Keep up the great job you are doing!

FelCom is looking for a webmaster to monitor the [Bethesda Postdocs Facebook group page](#) and to update the [FelCom webpage](#). This is an excellent opportunity to use your social media skills and to add communication experience to your resume! Contact the Social Committee co-chairs [Yingxi Chen](#) and [Steven Brooks](#) for more information.

Have you checked out the [Career Center of National Postdoctoral Association](#)? It's an international job database that you can join by uploading your CV/resume to start finding job opportunities.

The Career Development Subcommittee is concluding their events for the 2018-2019 term with a panel on "Careers in Contract Research Organizations (CRO's)." The event will be listed in the OITE Upcoming Events page and is scheduled to take place on **April 16, 3 to 5 p.m., in Building 40, room 1201.**

The Service and Outreach Subcommittee has reserved space for 10 fellows on the Casey Trees event "[Park Inventory: Kalorama Park](#)." It will take place on June 1, and information on how to register will be distributed through Felcom-L listserv in April and May.

Have a happy April!





Life Outside Lab  
*Pi Day*  
*Pie Competition*  
MARCH 14, 2018



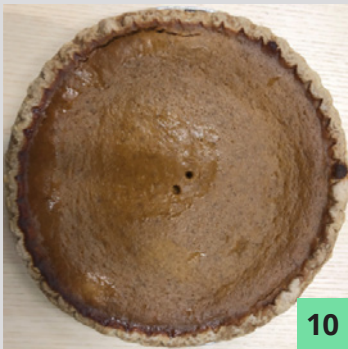
The NICHD Worklife Enrichment (WE) Committee hosted its annual pie bake-off celebration commemorating the mathematical constant pi on March 14, 2019. With 15 pies submitted, the participants faced stiff competition!

**AND THE WINNERS ARE...**

**First Place:** Jacob Balenson (Duck Pie)  
**Second Place:** Adam Habibi (Cranberry Cheesecake Pie)  
**Third Place:** Angie Wish (Salted Turtle Cream Cheese Pie)

**Most Unique:** Roshonna Davis (Lemon Lush Pie)  
**People's Choice:** Mahua Mukhopadhyay (Chickpea Curry Pie)

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## Upcoming NIH-Wide Office of Intramural Training and Education (OITE) Events

For more information and registration, please visit [Upcoming OITE Events](#).

Job Search Strategies (April 2)  
 Creating and Presenting Dynamic Posters (April 4)  
 Industry: Negotiating Offers and Making the Transition (April 9)  
 Succeeding in Graduate School (For Future Graduate Students) (April 10)  
 Tips for Mentoring a Summer Intern and Leading a Summer Journal Club (April 11)  
 Workplace Dynamics V: Diversity in a Multicultural Society (April 12)  
 Postbac Seminar Series (April 16)  
 Academics: Transitioning Successfully from Postdoc to Faculty (April 17)

## Pi Day Key

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- |  |  |
|--|--|
| 1. French Coconut Raspberry Pie            | 8. <b>Salted Turtle Cream Cheese Pie</b> |
| 2. Sweet Potato Buttermilk Pie             | <b>Third Place: Angie Wish</b>           |
| 3. <b>Chickpea Curry Pie</b>               | 9. Peanut Butter Pie                     |
| <b>People's Choice: Mahua Mukhopadhyay</b> | 10. Pumpkin Pie                          |
| 4. <b>Cranberry Cheesecake Pie</b>         | 11. Chocolate Banana Nut Pie             |
| <b>Second Place: Adam Habibi</b>           | 12. Pumpkin Slab                         |
| 5. <b>Duck Pie</b>                         | 13. <b>Lemon Lush Pie</b>                |
| <b>First Place: Jacob Balenson</b>         | <b>Most Unique: Roshonna Davis</b>       |
| 6. Strawberry Crumble Pie                  | 14. Pineapple Pudding Pie                |
| 7. Cranberry Almond Apple Pie              | 15. Chocolate & Cherry Pie               |



## April Announcements

### REGISTRATION OPEN FOR ANNUAL NICHD FELLOWS MEETING

Registration is LIVE at <http://retreat.nichd.nih.gov>. Don't delay!

The 15<sup>th</sup> Annual Meeting for Postdoctoral, Clinical, and Visiting Fellows and Graduate Students will take place on **Friday, May 31, 2019**. This year's retreat will be held at the William F. Bolger Center in Potomac, MD.

This meeting will allow you to step away from the lab for a day to network with your NICHD colleagues, participate in a career exploration session, and learn more about the recent developments in our intramural research programs.

This year's retreat will include:

- » Keynote Address by **Dr. Elaine Ostrander**, NIH Distinguished Investigator, Cancer Genetics and Comparative Genomics Branch, National Human Genome Research Institute
- » **Career breakout sessions** with professionals from academe, industry, teaching, government administration, science communications, science policy, grants management, and technology transfer
- » Afternoon presentation by **Dr. Mark Stopfer**, NICHD Senior Investigator, Unit on Sensory Coding and Neural Ensembles
- » You can be a highlight at the retreat too! You can present your work during the poster session, and six fellows will be selected to give a talk from their submitted abstracts.

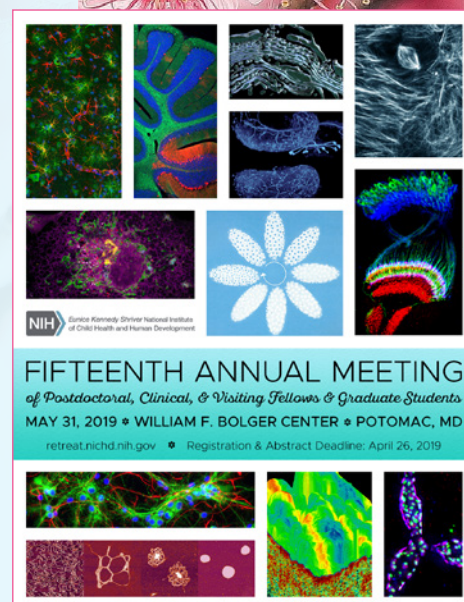
Don't forget to sign up early; space is limited to **110 fellows**!

### ARE YOU A BUDDING PHOTOGRAPHER? CHECK THIS OUT

The NICHD Office of Education is seeking a fellow with photography experience for the upcoming fellows retreat. Your photography of the event will appear in the retreat recap issue of *The NICHD Connection* this summer. If you are interested, please contact Nicki Swan ([jonasnic@mail.nih.gov](mailto:jonasnic@mail.nih.gov)) for additional details.



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## April Announcements

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### COMMUNICATE YOUR RESEARCH TO THE PUBLIC

Did you know? The NICHD Office of Communications posts intramural research findings on the institute's social media accounts. They're looking for fellows to discuss their work and pose for pictures in the lab, to offer a behind-the-scenes look at research. If you are interested or have biomedical art images to share, please contact Linda Huynh, PhD, at [linda.huynh@nih.gov](mailto:linda.huynh@nih.gov).

If you have an accepted manuscript that is potentially newsworthy for the general public, please email the office's press team at [nichdpress@mail.nih.gov](mailto:nichdpress@mail.nih.gov) before the paper is published. Include a copy of the manuscript and a brief, plain language explanation on why the work is important.

### RESPONSIBLE CONDUCT OF RESEARCH TRAINING FOR NEW NICHD POSTDOCS

**"Discussion of Ethical Research Practices: Making Good Choices"**

**Wednesday, May 22, 1 – 2:30 p.m.**

***This mandatory training is for all postdocs who started after January 1, 2018.***

An interactive session that promotes both self-directed and team-based learning required for all new postdoctoral fellows, through the Office of Education. Led by the Office of Education, this session will include case studies and reading assignments related to research integrity and discussions on ways to reduce risk factors.

The session will begin with a brief discussion on pre-assigned reading materials, followed by small-group, team-based learning exercises involving complex cases that promote discussions of either fabrication, falsification, plagiarism, mentoring expectations, and/or trainee responsibilities. The workshop will include good practices of data management and presentation, including lab notebook management—both physical and electronic. For additional details and to register, contact Dr. Erin Walsh at [erin.walsh@nih.gov](mailto:erin.walsh@nih.gov).

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## April Announcements

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### **DUE THIS MONTH: GENETICS POLICY AND EDUCATION FELLOWSHIP APPLICATIONS**

*The deadline for applications is Friday, April 19, 2019.*

The Genetics and Public Policy Fellowship is designed as a bridge for genetics professionals wishing to transition to a policy career. This unique fellowship provides three separate types of policy experience: within NHGRI's Policy and Program Analysis Branch; on Capitol Hill serving elected officials in the Legislative Branch; and at ASHG in the non-profit science advocacy sector.

The Genetics Education and Engagement fellowship program is designed for genetics professionals (or life scientists with substantial experience in genetics or genomics) who: have an advanced degree, are early in their careers, and are interested in developing and implementing genetic and genomic literacy, engagement, diversity, and/or professional development initiatives for audiences at all educational or career levels. The fellow will participate in rotations at the NHGRI and ASHG, and typically a third organization involved in genetic and genomic literacy, engagement, diversity, or professional development.

For more information, and to apply, visit [Genetics & Public Policy Fellowship](#) and [Genetics Education & Engagement Fellowship](#).

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## April Announcements

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### RECRUITING NICHD POSTDOC & GRADUATE STUDENT JUDGES FOR THE 2019 NIH POSTBAC POSTER DAY!

Please contact Dr. Erin Walsh at [erin.walsh@nih.gov](mailto:erin.walsh@nih.gov) if you would like to help judge the NICHD postbaccalaureate fellows' posters in May. We would like to recruit a few postdoc and graduate student judges to visit about five posters each and attend a meeting to select the three “best poster” winners for 2019. This can be a great learning experience for both the judges and postbac trainees!

**Postbac Poster Day will take place on Thursday, May 2, at the Natcher Conference Center (Building 45) from 10:00 a.m. to 3:30 p.m.** For more information about the event, please visit [https://www.training.nih.gov/postbac\\_poster\\_day](https://www.training.nih.gov/postbac_poster_day).

### SAVE THE DATE: NEXT NICHD FELLOWS ADVISORY COMMITTEE MEETING

Thursday, May 2, 3 – 4 p.m.

The committee meets monthly to exchange ideas and informally discuss ways we can enhance and tailor the training experience within the NICHD intramural. Please contact Dr. Erin Walsh at [erin.walsh@nih.gov](mailto:erin.walsh@nih.gov) if you are interested in joining the group.



## April Events

**MONDAY, APRIL 17, 12 NOON – 1 PM**

**Lunchtime Session for Postbacs:  
Applying to PhD and MD/PhD Programs**

NICHD postbacs who were recently accepted into PhD or MD/PhD programs will share with you their application and interviewing experiences. This will be a casual discussion and Q&A session.

Topics may include: what to consider when selecting programs to apply to; tips for preparing a strong application; interviewing tips and strategies; key factors to consider when choosing a program; how to handle being wait-listed; and what panelists wish they had known or done differently during the process. Feel free to come prepared with your own questions!

To register, contact Dr. Erin Walsh ([erin.walsh@nih.gov](mailto:erin.walsh@nih.gov)).

**THURSDAY, APRIL 25, 9 AM – 4 PM**

**NIH 24<sup>th</sup> Annual "Take Your Child to Work Day"**

Bring your children in grades 1-12 and inspire them to explore career paths in science and public service at our nation's biomedical research agency. Together, you and your children can choose from over 100 activities, from exploring NIH labs and technology, to being a hands-on genetic researcher, to learning about the day-to-day life of social workers, chemists, dieticians, peer reviewers and more. Activities are available at on- and off-campus locations.

Children in grades 6-12 will also be able to register to volunteer to help with activities and may be able to earn Student Service Learning (SSL) credit, if offered by your school or school district. Please check with your school's SSL coordinator to find out if this volunteer opportunity meets your school's requirements.

Encourage your co-workers, your supervisor, and your colleagues/friends to participate and mark your calendars. Key registration dates are listed below:

**April 4 at 12 noon:** Registration Phase 1 (Register child/ren for up to 2 limited space activities each).

**April 10 at 12 noon:** Registration Phase 2 (Register child/ren for up to 2 additional limited space activities for a maximum of 4 limited space activities).

The Office of Research Services, Program and Employee Services is the primary sponsor of TYCTWD 2019. Please e-mail any questions and comments to [Take-Your-Child-To-Work@nih.gov](mailto:Take-Your-Child-To-Work@nih.gov).

If you are on Twitter, please follow [@NIHEmplSrvcs](https://twitter.com/NIHEmplSrvcs) for more TYCTWD information and announcements (by using [#MyNIHDay](https://twitter.com/MyNIHDay)), plus find out about all of the other employee services we provide to assist you with balancing work and family.

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## April Events

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**FRIDAY, APRIL 26**

### **Three-Minute Talks (TmT)**

Individual coaching/practice sessions with Scott Morgan. Practice your talk and obtain feedback on oral presentation skills and speech development.

This event requires registration. For more information, please contact Dr. Erin Walsh at [erin.walsh@nih.gov](mailto:erin.walsh@nih.gov).

The NICHD and NIH TmT competitions will be held on Wednesday, May 8, and Thursday, June 27, respectively.